

REMARKS

Entry of the foregoing, reexamination and further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested.

The Office Action Summary correctly indicates that claims 46-70 are pending in the application. Claims 46-70 are subject to a restriction requirement. Claims 57-70 have been withdrawn from consideration. Claims 46-56 are under consideration and stand rejected.

Claim 46 has been amended to more clearly describe the final product of the claimed method. Support for the amendments to claim 46 can be found in the specification at least at page 6, lines 12-20, and at page 7 lines 14-26. That the recited properties are those of the final preparation and not an, as recited in amended claim 46, is described throughout the specification in that preparations having the properties recited in claim 46 are described as being used in a variety of biochemical assays.

No prohibited new matter has been introduced by way of the above amendments. Applicants reserve the right to file a continuation or divisional application on subject matter canceled by way of this Amendment.

Examiner Interview

Applicants' Representative thanks the Examiner and his supervisor for the courtesy of a telephonic interview on January 8, 2007. The amendments presented herein were discussed with regard to the Examiner's remarks at page 4 of the Office Action. Applicants representative also presented arguments substantially as set forth below, and the examiner agreed to reconsider the rejection in light of these amendments and arguments.

Rejections under 35 U.S.C. § 103

Claims 46-56 stand rejected under 35 U.S.C. § 103 as allegedly unpatentable over Reddy and Sastry (Brain Research, 168:287-98, 1979) in view of Israel et al. (Biochem.J. 160:113-15, 1976). Claim 46 has been amended. Each of claims 47-56 depend directly or indirectly upon claim 46. To the extent that the rejection might be alleged against the claims as amended, the rejection is traversed.

The prior art fails to establish a proper prima facie case of obviousness. To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

M.P.E.P. § 2143.

The prior art does not teach or suggest the invention as presently claimed. Furthermore, there could not have been any motivation to modify the prior art as the Office has suggested, because to do so would have gone against the stated purpose of the reference cited by the Office and against the conventional wisdom in the art. Reddy and Sastry were previously cited by the Office in a rejection under 35 U.S.C. § 102 that has been withdrawn. Reddy and Sastry describe passing minced brain tissue in Krebs-Ringer bicarbonate solution ten times through nylon bolting cloth having mesh sizes of 433 μm , 264 μm , 130 μm , and 44 μm successively in decreasing order of pore size. Reddy and Sastry does not teach or suggest using any larger mesh.

The claims have been amended to more clearly show the differences between the methods of the present invention and the prior art. Specifically, by the present amendment,

claim 46 has been amended to recite a final step of harvesting the calibrated pieces of mammalian cerebral tissue produced in step (iv) so that the final preparation comprises calibrated pieces of mammalian cerebral tissue having a mean size between 0.1 mm³ and 5 mm³ wherein at least some connections between neurons are maintained. Thus the claim indicates that that the final product of the method, which is ready to be used in the assay methods described in the application has the properties produced by step (iv), which applicants have proven is different from the pieces of tissue produced by the methods of Reddy and Sastry. The claimed methods do not include proceeding to pass the sample through the smaller meshes taught by the prior art, which would necessarily produce a synaptosome tissue preparation.

Synaptosome preparations are quantitatively and qualitatively different from a preparation of tissue such as produced by the presently claimed methods, which comprises pieces of a size to comprise neurons wherein at least some of the connections between neurons have been maintained. Applicants have previously presented evidence that the method taught by Reddy and Sastry necessarily results in a preparation that is structurally and functionally distinct from the preparation taught and claimed in the present application. Dr. Israel testified that the method of Reddy and Sastry would produce a synaptosome preparation containing pinched-off nerve terminals. Such preparations were commonly used in the prior art as the conventional wisdom taught the use of synaptosomes for conducting experiments in tissue suspensions.

The Office has acknowledged that Reddy and Sastry do not teach the use of a mesh size that could produce the calibrated pieces of tissue recited in the claims. However, in this new ground of rejection, the Office has alleged that it would be obvious to combine the teaching of Israel et al. with Reddy and Sastry. Israel et al. passed chopped pieces of the

electric organ of *Torpedo mamorata* through grids of 1000, 500, and 200 μm in that order.

The Office has alleged that it would have been obvious to use the 1000 μm grid taught by Israel et al. in the method of Reddy and Sastry to make a preparation of calibrated pieces of mammalian brain tissue as recited in the claims as previously presented.

Even if the references were combined, a person of ordinary skill would not have been motivated to practice the claimed invention. Applicants respectfully submit that the Office is in error in asserting that it is irrelevant that Israel et al. passed the pieces of neural tissue through grids smaller than 1000 μm . This is because neither Israel et al. or Reddy and Sastry taught or suggested harvesting calibrated pieces of mammalian cerebral tissue having a mean size between 0.1 mm^3 and 5 mm^3 . Even if a person of skill in the art were to combine the teachings of Israel et al. and Reddy and Sastry, that person would have been led to continue passing the tissue through successively smaller mesh grids as taught in both Israel et al. and Reddy and Sastry. The result of the combined teaching would have been substantially different from the presently claimed invention.

One would not have been led to harvest calibrated pieces of mammalian cerebral tissue having a mean size between 0.1 mm^3 and 5 mm^3 as recited in the present claims, because to do so would have gone against the conventional wisdom in the art exemplified by Reddy and Sastry and Israel et al. that studies on neurotransmitter effects should be carried out using synaptosome preparations as was testified to by Dr. Israel, that is to make preparations of tissue using successive passages through smaller mesh grids than in the present invention. There could not have been any motivation to modify the prior art in the manner proposed by the Office, because to do so would have been contrary to the accepted wisdom in the art.

Moreover, the stated purpose of Israel et al was contrary to the modification that the Office has proposed. The stated purpose of Israel et al. was to make a preparation of synaptosomes, that is a preparation of pinched-off nerve terminals. Doing so required the use of successively smaller mesh grids. It could not have been obvious to choose to use only part of the teaching of Israel et al., when doing so would have defeated the stated purpose of the reference.

Neither Israel et al. nor Reddy and Sastry teach or suggest harvesting calibrated pieces of mammalian cerebral tissue having the recited size so that the final preparation comprises calibrated pieces of mammalian cerebral tissue comprising neurons, wherein at least some of the connections between neurons are maintained.

Finally, the Office is reminded that an analysis of obviousness of a claimed invention must include consideration of the results achieved by that invention. *The Gillette Co. v. S.C. Johnson & Son Inc.*, 16 USPQ2d 1923, 1928 (Fed. Cir. 1990). Critical to the analysis is an understanding of the particular results achieved by the invention. *Id.* (citing *Interconnect Planning Corporation v. Feil*, 227 U.S.P.Q. 543, 551 (Fed. Cir 1985)). Applicants have presented the testimony of Dr. Israel, who explained the surprising benefits of using a preparation made according to the methods of the present invention. The prior art simply did not appreciate the benefits of the presently claimed methods for preparing aliquots of tissue. The presently claimed methods provide capabilities never before achieved in advancing the field of study of neuromodulators.

For at least the foregoing reasons, the claimed invention is not rendered obvious by the prior art. Accordingly, withdrawal of the rejection is respectfully requested.

CONCLUSION

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned concerning such questions so that prosecution of this application may be expedited.


The Director is hereby authorized to charge any appropriate fees that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800.

Respectfully submitted,

BUCHANAN INGERSOLL & ROONEY PC

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